MS APPEAL BRIEF - PATENTS
PATENT
0020-4559P

IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant:	Eijiro WATANABE et al.	Conf.:	6045
Appl. No.:	09/301,766	Group:	1638
Filed:	April 29, 1999	Examiner:	D. KRUSE
For:	RAFFINOSE SYNTHASE GENES AND THEIR USE		

REPLY BRIEF
FILED UNDER PROVISIONS OF 37 C.F.R. § 41.41

MS Reply Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Appellants' Reply Brief responsive to new arguments presented in the Examiner's Answer of January 30, 2008 is provided.

REPLY BRIEF

Appellants address new arguments raised by the Examiner in his Answer of January 30, 2008. Each new argument is addressed in turn.

A. The Examiner fails to find support for certain features in the claims, and other assertions by the Examiner of inadequacy of the written description

At page 9 of the Examiner's Answer, the Examiner indicates that he, "cannot find Appellants' asserted support for constrained amino acid sequences of a RFS at pages 20-21 of the specification which describes degenerate PCR primers. The Examiner overlooks that the degenerate primers described at this part of the specification span regions of conserved amino acid sequence that they encode.

Appellants further assert that the *Wallach* case cited by the Examiner is distinguishable from the facts of the present application. At least, as noted by the Examiner, in *Wallach* there was no knowledge, in either the prior art or in the specification, of the amino acid sequence of the protein in question. In the instant case, raffinose synthases had been characterized in the prior art, and the instant specification provides the complete amino acid sequence of an enzyme demonstrated to have raffinose synthase (RFS) activity (SEQ ID NO: 5). The instant specification further provides the complete amino acid sequence of at least one variant RFS obtained from a different species of plant (SEQ ID NO: 3), and also partial amino acid sequences from two additional species of plants (SEQ ID NOS: 1 and 7). Thus, there is ample disclosure in the present specification that guides the artisan of ordinary skill to portions of the amino acid sequence of a raffinose synthase that are conserved across diverse species and so are likely to be required for RFS activity. The Board might also consider disclosure in the specification at page 15, line 5 to page 16, line 7, also expressly disclosing portions of RFS sequence having a high degree of sequence identity to SEQ ID NO: 5. The specification at this point also informs the reader that sequence identity to the recited degree indicates likelihood that a protein having such a homologous sequence can be identified as a RFS enzyme (page 15, lines 3-4).

At page 11 of the Examiner's Answer, the Examiner asserts that under the holding of *University of California v. Eli Lilly & Co.*, 43 USPA2d 1398 (Fed. Cir. 1997), disclosure only of a process for obtaining a cDNA from a particular organism is inadequate written description of an actual cDNA from that organism that would encode a protein from that organism. Again, the facts of the present application are easily distinguished from those of *Lilly*.

First, the present claims do not broadly recite a "vertebrate" or "mammalian" cDNA encoding a particular protein. Rather, the present claims either recite a cDNA having a particular nucleotide sequence or encoding a particular amino acid sequence (e.g. parts (a) to (f) of claim 1), or recite a cDNA obtained as a product of a process (e.g. claim 1, parts (g) and (h)), wherein particular PCR primers are used to amplify template nucleic acids obtained from plants of recited kinds.

Second, as explained above, the present application provides the complete cDNA sequence of two variants of RFS from plants (SEQ ID NOS: 4 and 6) and cDNA sequences encoding the majority of the amino acid sequence for yet two more RFS enzymes from two other plants (SEQ ID NOS: 2 and 8). Furthermore, as explained above, by disclosing PCR primers designed by examination of nucleotide sequences obtained from the cloning efforts disclosed in the present application, which represent regions of amino acid sequence conserved among various RFS sequences, the present application discloses regions of amino acid sequence conserved among a number of raffinose synthase enzymes and so thought necessary for activity. Furthermore, the disclosed PCR primers were used to isolate cDNAs from the corresponding genes from diverse plant species. In contrast, the disclosure in *Eli Lilly* that the patentee relied upon was merely of an amino acid sequence of a human protein and a single cDNA sequence of a corresponding protein from a rat. There was no evidence presented by the specification that any part of the rat cDNA could be used to obtain the cDNA of the human gene.

Thus, the present claims and the amount of disclosure supporting them are so distinct from those at issue in *Eli Lilly* that the case is wholly inapplicable to the present application.

At page 16, 1st paragraph of the Examiner's Answer, the Examiner asserts that the copending application does not share common priority with the instant application nor is there a claim to priority in the instant application to the copending application, and therefore the Appellant cannot

rely upon disclosure in the copending application for written description support of the present claims.

The copending application may not be available for written description per se, but it does reflect the state of the art at the time the present application was filed. Such is the "starting point" from which the disclosure must describe the invention. See, *Capon v. Esshar*, 76 USPQ2d 1078 (Fed. Cir. 2005) and *Faulkner v. Inglis*, 79 USPQ2d 1001 (Fed. Cir. 2006) which establish the rule that the written description should not be viewed in isolation, but the state of the art must also be considered.

B. The Examiner asserts that the utility of the presently claimed invention is not enabled

The recent case of *Ex parte Kubin*, 83 USPQ2d 1410 (BPAI 2007) is directly on point with respect to the issue of enablement. In *Kubin*, after considering the "Wands factors" in view of the prior art teachings relied upon by the Appellant and by the Examiner, which included publications describing unpredictability in the art with respect to variation of protein sequences and retention of biological function, the Board found:

> We agree with the Examiner that molecular biology is generally an unpredictable art (and thus was so at the time the application was filed.) However, with respect to enablement, the other *Wands* factors weigh in Appellants' favor, particularly 'the state of the art' and 'the relative skill of those in the art,' [cite omitted], as evidenced by the prior art teachings and Appellants' Specification.
>
> The amount of experimentation to practice the full scope of the claimed invention might have been extensive, but it would have been routine. The techniques necessary to do so were well known to those skilled in the art.

Kubin, at page 1416.

As has been repeatedly asserted by Appellants, the present specification well describes methods for making variants of the proven operable SEQ ID NO: 5 and testing them for activity as a RFS enzyme. See the working examples 1-5 and the disclosure at page 26, lines 13 and following of

how to test an enzyme encoded by a cloned cDNA for RFS activity (reference to Lehle and Tanner, of record).

Appellants would pre-empt any adverse application of *Kubin* to the written description rejection in the instant case.

In *Kubin* all of the amino acid sequences of NAIL proteins that were presented in the specification were identical as to amino acids 22-221 of SEQ ID NO: 2, the mature NAIL protein sequence (ff 20-22). These facts must be contrasted to the instant application, in which two full-length amino acid sequences, of RFS enzymes of two different plant genera and two partial amino acid sequences, representing about 75% of the protein, of RFS enzymes from yet two more plants, from yet two more genera, are presented.

In *Kubin*, the Board took pains to explain that the patent did not disclose any structure that was correlated with activity of the NAIL protein, and further that, "if the functional characteristic of ...binding to [CD 48] were coupled with a disclosed correlation between that function and a structure that is sufficiently known or disclosed, the written description requirement may be met."

The Board should note then that the present specification discloses portions of the RFS enzyme amino acid sequence that are conserved across species, perhaps genera in some instances. The presence of these sequences in a protein "confirms" the protein is a RFS enzyme. Thus, the presence of these sequences is correlated with raffinose synthase enzyme function. See, e.g. pages 15-16 of the specification as explained above.

At page 23 the Examiner responds to Appellant's arguments that the specification describes making variants of RFS and testing them for activity, e.g. expression of the RFS cDNA and testing for raffinose synthase activity in the expressed polypeptide by a disclosed assay by asserting that Appellants' arguments related to, "limitations not stated in the claims." This is completely irrelevant; that is an issue with respect to distinguishing the claims from prior art. The Examiner's assertion is also factually incorrect.

The claims are not required to recite features needed for enablement that go beyond structures required for operability. Here the question is whether the specification provides sufficient description to allow the skilled artisan to make and use the invention that is recited in the claims

throughout the scope of the claims. Furthermore, features linked to the enablement arguments are recited in the claims, for instance, the activity of the protein, and (in some dependent claims) use of specific primers.

The Examiner argues at page 24 of the Examiner's Answer that the specification does not disclose any conserved structural feature. Again the Examiner is misapplying a rule for another statutory requirement. Disclosure of conserved structural features is a consideration of adequate written description, not for enablement. Also, the Examiner's argument is factually incorrect, as has been pointed out many times, at least with reference to disclosure at, e.g. pages 15-16 and 20-21 of the application.

Among pages 31-33 of the Examiner's Answer, the Examiner fails to provide any "reason above" why the alternate utilities (to altering raffinose synthase activity in a plant) asserted in the specification are not persuasive. (See, the end of paragraphs VIIB.3., .5. and .6..) Also, the Examiner generally fails to address the argument that narrower claims, thus encompassing only subject matter more clearly distinguishable from a stachyose synthase enzyme, are more easily found enabled if the failure of enablement relates to the likelihood that a structural prediction of one enzyme activity over another is correct.

The Examiner would frame the issue for consideration of the rejection under 35 USC § 112, first paragraph as, "whether the instant specification actually teaches more than one actual raffinose synthase encoding polynucleotide" (page 23, last two lines, of the Examiner's Answer), in view of the disclosure in the specification, and the data and other evidence of record. Appellants submit that the answer is that the evidence of record meets Appellants burden of proof that it is more likely than not that the specification discloses at least two raffinose synthase encoding polynucleotides, and discloses two more polynucleotides that encode most of a raffinose synthase enzyme that provide the starting materials to obtain the remainder using known and disclosed techniques so as to complete a polynucleotide encoding a raffinose synthase enzyme.

Furthermore, the specification discloses portions of the amino acid sequences presented that are correlated with function of the polypeptide as a raffinose synthase enzyme, and provides both

methods and starting materials for making variants of the disclosed amino acid sequences and testing them for activity as raffinose synthase enzymes. The disclosure of the specification, taken with what was known in the art at the time the application was filed, is sufficient to demonstrate both possession of the claimed invention throughout its scope at the time of filing, and also to enable the artisan of ordinary skill to practice the invention throughout its claimed scope. Thus, the specification is adequate to support the claims from the standpoints of both written description and enablement.

For all of the reasons set forth hereinabove, in Appellants' primary Appeal Brief, and in Appellants' papers of record, the Examiner's decisions rejecting claims 1, 4, 5, 8-10, 16-23 and 28-29 under 35 USC § 112, first paragraph, for lack of adequate written description support and enablement in the specification, should be revered. Such favorable action and the allowance of claims 1, 4, 5, 8-10, 16-23 and 28-29 are respectfully requested.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Date: March 31, 2008

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By /mjn/
Mark J. Nuell, Ph.D., 36,623

12770 High Bluff Drive, Suite 260
San Diego, CA 92130
(858) 792-8855